UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/901,782	07/09/2001	Susan Hardin	0007/01UTL	9388

7590 12/12/2007

Robert W. Strozier
ROBERT W. STROZIER, P.L.L.C.
P.O. Box 429
Bellaire, TX 77402-0429

EXAMINER	
SISSON, BRADLEY L	
ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
12/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/901,782	HARDIN ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10,13,16-19,50-56,64-74,76-92,94-100 and 102-107* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,13,16-19,50-56,64-74,76-92,94-100 and 102-107* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *June 13 & 18, 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Location of Application

1. The location of the subject application has changed. The subject application is now located in Workgroup 1630, Art Unit 1634, and has been docketed to Primary Examiner Bradley L. Sisson.

Rejection under 35 U.S.C. 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claim s 19, 56, 70, 78, 88, and 99 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New Matter.

4. Claims 19, 56, 70, 78, 88, and 99 all refer to a collection of amino acid positions of SEQ ID NO. 11. Claim 19 is exemplary, and for convenience, is reproduced below.

19.(previously presented) The composition of claim 13, wherein the polymerase comprises *Taq* DNA polymerase I having a tag attached to an amino acid at a specific amino acid position of the *Taq* DNA polymerase I, where the amino acid position is selected from the group consisting of 513-518, 643, 647, 649 and 653-661 of SEQ. ID No. 11, where the tag comprises a fluorescent molecule.

5. A review of the application finds that the application was originally filed with a Sequence Listing that contained 48 sequence listings, and had the following for SEQ ID NO. 11:

```
<210>  11
<211>  36
<212>  DNA
<213>  Thermus aquaticus

<220>
<221>  Mutation
<222>  (22)..(24)
<223>  Taq Pol I Mutation Complimentary Strand: AA Site 652 glu to
cys:
       antisense codon: ctc -> gca.  5' to 3' listing.


<400>  11
gcgcatcagg gggtccacgg cgcaccgggg gacgcc
   36
```

6. A review of the current Sequence Listing finds that SEQ ID NO. 11 is not some 832 amino acids in length. Further, a review of the original Sequence Listing fails to find where applicant had disclosed under any SEQ ID NO. a protein that was 832 amino acids in length.

7. A review of the file history fails to find where applicant contemplated, and properly incorporated by reference, the now disclosed amino acid sequence.

8. It is further noted that upon review of the disclosure, applicant had contemplated various mutants of Taq polymerase, and at no time was this specific amino acid sequence disclosed. In view of the apparent addition of this sequence to the disclosure, the specification and claims 19, 56, 70, 78, 88, and 99 are deemed to comprise new matter.

9. Claims 10, 17, and 18 have been construed as encompassing a "polymerizing agent" that would serve to polymerize nucleotides, but also any other polymer, be it a

cellulose, plastics, rubber, lipoproteins, etc. A review of the disclosure fails to find where applicant had contemplated these alternative embodiments and had provided such full, clear, and concise description of the compounds, and of the methods for making and using same, so as to reasonably suggest that applicant had possession of the full genus encompassed by the claims.

10. Attention is directed to the decision in *In re Shokal*, 113 USPQ 283 (CCPA 1957) wherein is stated:

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.
>
> ***
>
> We are of the opinion that a genus containing such a large number of species cannot properly be identified by the mere recitation or reduction to practice of four or five of them. As was pointed out by the examiner, four species might be held to support a genus, if such genus is disclosed in clear language; but where those species must be relied on not only to illustrate the genus but to define what it is, the situation is otherwise.

11. Applicant is urged to consider narrowing the claims to those embodiments where the polymer is a nucleic acid and the "polymerizing agent" is a polymerase.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 10, 16, 17, 18, 50, 64, 68, 71, 79, 89, 96, 97, 100, 105, and 106 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

14. Claims 10, 16, 17, 18, 50, 64, 68, 71, 79, 89, 96, 97, 100, 105, and 106 are indefinite with respect to just what constitutes the metes and bounds of a "polymerizing agent."

15. Claim 17 recites the limitation "the polymerase tag" in line 2. There is insufficient antecedent basis for this limitation in the claim.

16. Claim 55 recites the limitation "the polymerase tag" in line 2. There is insufficient antecedent basis for this limitation in the claim.

17. Claim 69 recites the limitation "the polymerase tag" in line 2. There is insufficient antecedent basis for this limitation in the claim.

18. Claim 77 recites the limitation "the polymerase tag" in line 2. There is insufficient antecedent basis for this limitation in the claim.

19. Claim 87 recites the limitation "the polymerase tag" in line 2. There is insufficient antecedent basis for this limitation in the claim.

20. Claim 98 recites the limitation "the polymerase tag" in line 2. There is insufficient antecedent basis for this limitation in the claim.

21. Claim 102 recites the limitation "the polymerase" in line 1. There is insufficient antecedent basis for this limitation in the claim.

22. Claim 103 recites the limitation "the polymerase" in line 1. There is insufficient antecedent basis for this limitation in the claim.

23. Claim 104 recites the limitation "the polymerase" in line 1. There is insufficient antecedent basis for this limitation in the claim.

24. Claim 107 is confusing in that claim 13 from which it depends recites a polymerase, yet claim 107 uses the indefinite article "a." Is the polymerase of claim 107 a different polymerase from that recited in claim 13, or is it the same?

Claim Rejections - 35 USC § 102/103

25. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

26. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

27. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

28. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

29. Claims 10, 13, 17, and 18 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent 6,982,146 B1 (Schneider et al.).

30. It is noted that while Schneider et al., was published 03 January 2006, it claims benefit of priority to provisional application 60/151,580, filed 30 August 1999. In comparison, the instant application claims benefit of priority to provisional application filed 07 July 2000. Accordingly, Schneider et al., qualifies as 102(e)-type art.

31. Schneider et al., disclose methods, and related compositions, for conducting sequencing reactions. As seen at column 5, the polymerase and nucleotides are both labeled, and that either can serve as a donor or acceptor of a signal, which can be fluorophores.

32. Schneider et al., column 9, teach explicitly of the application of fluorescence resonance energy transfer (FRET).

33. Schneider et al., column 10, teaches that "[o]ne of ordinary skill in the art can easily determine...which fluorophores will make suitable donor-acceptor FRET pairs.

34. Schneider et al., column 13, disclose a plethora of polymerizing agents.

35. Schneider et al., column 25, teach that the fluorophore can be linked directly or indirectly to the nucleotide.

36. Schneider et al., column 9, teach that the donor and acceptor fluorophores need to be within 10 to 100 Angstroms of one another for fluorescence resonance energy transfer to take place.

37. In view of the above remarks, and in the absence of convincing evidence to the contrary, claims 10, 13, 17, and 18 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent 6,982,146 B1 (Schneider et al.).

38. Claims 16, 19, 50-56, 64-74, 76-92, 94-100, and 102-107 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,982,146 B1 (Schneider et al.) in view of US Patent 7,037,687 B2 (Williams et al.) and US Patent 5,849,478 (Cashman).

39. It is noted that while Schneider et al., was published 03 January 2006, it claims benefit of priority to provisional application 60/151,580, filed 30 August 1999. In comparison, the instant application claims benefit of priority to provisional application filed 07 July 2000. Accordingly, Schneider et al., qualifies as 102(e)-type art.

40. Schneider et al., disclose methods, and related compositions, for conducting sequencing reactions. As seen at column 5, the polymerase and nucleotides are both labeled, and that either can serve as a donor or acceptor of a signal, which can be fluorophores.

41. Schneider et al., column 9, teach explicitly of the application of fluorescence resonance energy transfer (FRET).

42. Schneider et al., column 10, teaches that "[o]ne of ordinary skill in the art can easily determine...which fluorophores will make suitable donor-acceptor FRET pairs.

43. Schneider et al., column 13, disclose a plethora of polymerizing agents, which include DNA polymerase I, Taq polymerase, reverse transcriptase, and RNA polymerase.

44. Schneider et al., column 25, teach that the fluorophore can be linked directly or indirectly to the nucleotide.

45. Schneider et al., column 9, teach that the donor and acceptor fluorophores need to be within 10 to 100 Angstroms of one another for fluorescence resonance energy transfer to take place.

46. While Schneider et al. disclose numerous polymerases, they do not teach specifically if the polymerases lack exonuclease activity.

47. Williams et al., column 4, teach that their method utilizes polymerases that are deficient in exonuclease activity.

48. Williams et al., column 7, disclose polymerases that are useful in such a procedure. As seen therein, one such polymerizing agent is *Taq* polymerase as well as T7 DNA polymerase, Klenow polymerase, reverse transcriptase, etc.

49. Williams et al., column 12, bridging to column 13, disclose using fluorescently-labeled nucleotides, and their being incorporated by the aforementioned polymerases.

50. Neither Schneider et al., nor Williams et al., have been found to disclose using nucleotide where the fluorescent label is attached to a terminal phosphate.

51. Cashman, column 12, teach explicitly of devising kits that comprise not only any of a variety of polymerases, but also nucleotides that bear a fluorescent label attached to a terminal phosphate.

52. It would have been obvious to one of ordinary ski in the art at the time the invention was made to have combined the compositions of Cashman with that of Williams et al., and Schneider et al., as such would have allowed the ordinary artisan to combined labeled polymerases with labeled nucleotides wherein the labels can be a member of a FRET pair, As the prior art teaches explicitly of using both these polymerases with terminal phosphate labeled nucleotides.

53. Neither Schneider et al., Williams, nor Cushman have been found to teach the specific amino acids positions of *Taq* polymerase recited in claims 19, 56, 70, 78, 88, and 99. The selection of which amino acid of *Taq* polymerase to be labeled is not deemed to constitute a patentable distinction as Schneider et al., column 9, teach that the donor and acceptor fluorophores need to be within 10 to 100 Angstroms of one another for fluorescence resonance energy transfer to take place. With Cashman teaching the use of terminal-phosphate labeled nucleotide, it would be a matter of routine experimentation and optimization to identify those amino acids that would result in the FRET pair being within the prescribed distance.

54. It is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

> Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. In re Dreyfus, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52; In re Waite et al., 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586. Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. In re Swenson et al., 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372; In re Scherl, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204. However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. In re Sola, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; In re Normann et al., 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; In re Irmscher, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Swain et al., 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; Minnesota Mining and Mfg. Co. v. Coe, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; Allen et al. v. Coe, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

55. Attention is directed to the decision in KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007)

> When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

56. For the above reasons, and in the absence of convincing evidence to the contrary, claims 16, 19, 50-56, 64-74, 76-92, 94-100, and 102-107 are rejected under 35 U.S.C.

103(a) as being unpatentable over US Patent 6,982,146 B1 (Schneider et al.) in view of US Patent 7,037,687 B2 (Williams et al.) and US Patent 5,849,478 (Cashman).

Conclusion

57. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

58. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

59. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO

Customer Service Representative or access to the automated information system, call

800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bradley L. Sisson/
Primary Examiner
Art Unit 1634

BLS